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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/079,949	02/19/2002	Ebrahim Zandi	13761-7064	6542

38706 7590 06/13/2007

FOLEY & LARDNER LLP
1530 PAGE MILL ROAD
PALO ALTO, CA 94304

EXAMINER	
PROUTY, REBECCA E	
ART UNIT	**PAPER NUMBER**
1652	

MAIL DATE	DELIVERY MODE
06/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/079,949	ZANDI ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,5-7,17-19 and 21-41* is/are pending in the application.

4a) Of the above claim(s) *24-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,5-7,17-19 and 21-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1, 3, 4, 8-16, and 20 have been canceled. Claims 2, 5-7, 17-19 and 21-41 are still at issue and are present for examination.

Claims 24-41 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse the response filed 10/4/04.

Applicants' arguments filed on 10/23/06, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 5-7, 17-19, and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Li et al. or Rothwarf et al. (Reference C27 of Applicant's PTO-1449) in view of Traincard et al. and Epinat et al. The rejection is explained in the previous Office Action.

Applicants argue that the combination of references fails to teach or suggest a method for reconstituting a substantially homogenous IKK protein complex comprising at least the IKKγ subunit. Applicants argue that mammalian systems as taught in the art do not form substantially homogenous complex because the exogenous IKK gene products complex with endogenously produced IKK gene products. However, this is not persuasive as the cited art clearly would have led a skilled artisan to reasonably expect that similar complications would not occur when the IKK complexes are produced in yeast as the art leads a skilled artisan to conclude that yeast do not endogenously produce IKK proteins. As such any IKK complexes formed would necessarily have to comprise only those IKK subunit proteins produced from the heterologously introduced IKK genes and therefore would be homogenous in composition.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system,

see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rebecca Prouty
Primary Examiner
Art Unit 1652

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/16/07 has been entered.

Claims 1, 3, 4, 8-16, and 20 have been canceled. Claims 2, 5-7, 17-19 and 21-41 are still at issue and are present for examination.

Claims 24-41 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse the response filed 10/4/04.

Applicants' arguments filed on 4/16/07, have been fully considered but are not deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at

> the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 5-7, 17-19, and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Li et al. or Rothwarf et al. (Reference C27 of Applicant's PTO-1449) in view of Traincard et al. and Epinat et al.

Each of Li et al. and Rothwarf et al. teach the coexpression of IKKα, IKKβ and IKKγ genes in a eukaryotic host by inserting the genes encoding each subunit fused to a tag (HA, FLAG or c-myc) into a mammalian expression vector, growing the host cell, lysing the host cell, and immunoprecipitating the IKK complexes. The only difference in the methods taught by Li et al. and Rothwarf et al. to the methods of the instant claims is that in the instant claims the expression host used is yeast.

Traincard et al. teach that within eukaryotic organisms, no homologs of any of member of the NF-κB signaling system (clearly disclosed as including Rel/NF-κB subunit genes, IκB subunit

genes and IKK genes) has been found within the genomes of *C. elegans* or *Saccharomyces cerevisiae* both of which were fully sequenced genomes at the time of publication of Traincard et al.

Epinat et al. teach that yeast is a convenient host for the reconstitution of the NF-κB system since it does not contain any endogenous NF-κB activity (see page 603) and that the reconstituted system provides an easy assay for testing stimuli or specific proteins that are postulated to be involved in NF-κB signaling (see page 609). Epinat et al. further suggest that yeast lack any endogenous IKK activity (see Figure 4 and page 609) and teach expression vectors for the recombinant expression of genes involved in the NF-κB signaling pathway in yeast cells under the control of both constitutive promoters such as the *ADH1* promoter and inducible promoters such as the *GAL1* promoter. The yeast expression vectors comprise selection markers such as the *URA3* or *LEU2* genes.

As the IKK complex is well known to be the part of the NF-κB signaling pathway responsible for IκB phosphorylation and as both Traincard et al. and Epinat et al. clearly suggest that yeast lack any endogenous IKK activity (as Traincard et al. teach that no IKK homologous genes were found in the yeast genome and Epinat et al. showed that an expressed IκB protein could not be phosphorylated in yeast even under similar stimuli

to those known to induce IκB phosphorylation in mammals) and as yeast are well known in the art to be the workhorse organism for the expression of eukaryotic proteins of interest, it would have been obvious to one of ordinary skill in the art to reconstitute the IKK complex in a yeast host cells by expressing the IKK subunit genes of Li et al. or Rothwarf et al. in yeast using any known yeast expression vector or yeast expression vectors as taught by Epinat et al.

Applicants argue that the combination of references fails to teach or suggest a method for reconstituting a substantially homogenous **and biologically functional** IKK protein complex as claimed because it was known at the time of the invention that yeast does not produce a homolog to the mammalian activating complex. However, this is not persuasive as both Li et al. and Rothwarf et al. clearly teach the importance of phosphorylation of the IKK complex for its kinase activity, teach that unstimulated cells producing the IKK complex still have a basal level of kinase activity and further teach that the IKK complex can be phosphorylated *in vitro* by the NIK and MEKK1 proteins to produce an active complex. As such one of skill in the art would reasonably expect that coexpression of the three subunits together in yeast would produce a complex that would have the basal level of kinase activity demonstrated by the unstimulated

cells of Li et al. and Rothwarf et al. and even if this in fact proved not to be the case a skilled artisan would have clearly expected that active complex could be produced by coexpression of either of NIK or MEKK1 in the yeast host as this is clearly taught by the art. As such the possible lack of the kinase(s) which phosphorylate the IKK complex *in vivo* in mammalian cells in yeast would not have prevented a skilled artisan from selecting yeast as a suitable host as the art clearly taught how to activate the complex if it was not active upon expression and coexpression of NIK or MEKK1 in the yeast is clearly not excluded from applicants claims.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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/Rebecca Prouty/
Primary Examiner
Art Unit 1652